

WHAT IS CLAIMED IS:

1. A pharmaceutical adenovirus composition comprising adenovirus particles and pharmaceutical excipients, the excipients including a bulking agent and one or more protectants, wherein the excipients are included in amounts effective to provide an adenovirus composition that is storage stable.
2. The adenovirus composition of claim 1, further defined as having an infectivity of between 60 and 100% of the starting infectivity, and a residual moisture of less than about 5%, when stored for six months at 4° centigrade.
3. The adenovirus composition of claim 1, further defined as a freeze dried composition.
4. The composition of claim 3, wherein the bulking agent is further defined as a bulking agent which forms crystals during freezing.
5. The composition of claim 1, wherein the bulking agent is mannitol, inositol, lactitol, xylitol, isomaltol, sorbitol, gelatin, agar, pectin, casein, dried skim milk, dried whole milk, silcate, carboxypolymethylene, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methhylcellulose or methylcellulose.
6. The composition of claim 5, wherein said bulking agent is mannitol.
7. The composition of claim 6, further defined as an aqueous composition comprising the bulking agent in a concentration of from about 1% to about 10% (w/v).
8. The composition of claim 7, wherein the aqueous composition comprises the bulking agent in a concentration of from about 3% to 8%.

18. The composition of claim 17, wherein the aqueous composition comprises the sugar in a concentration of from about 4% to 8%.

19. The composition of claim 18, wherein the aqueous composition comprises the sugar in a concentration of from about 5% to 6%.

20. The composition of claim 3, wherein the freeze dried composition was prepared from an aqueous composition comprising a non-reducing sugar in a concentration of from about 2% to 10% (w/v).

21. The composition of claim 20, wherein the freeze dried composition was prepared from an aqueous composition comprising a non-reducing sugar in a concentration of from about 4% to 8%.

22. The composition of claim 21, wherein the freeze dried composition was prepared from an aqueous composition comprising a non-reducing sugar in a concentration of from about 5% to 6%.

23. The composition of claim 13, wherein the cryoprotectant is niacinamide, creatinine, monosodium glutamate, dimethyl sulfoxide or sweet whey solids.

24. The composition of claim 1, wherein said protectant includes a lyoprotectant.

25. The composition of claim 24, wherein said lyoprotectant is human serum albumin, bovine serum albumin, PEG, glycine, arginine, proline, lysine, alanine, polyvinyl pyrrolidine, polyvinyl alcohol, polydextran, maltodextrins, hydroxypropyl-beta-cyclodextrin, partially hydrolysed starches, Tween-20 or Tween-80.

26. The composition of claim 25, wherein said lyoprotectant is human serum albumin.

27. The composition of claim 24, further defined as an aqueous composition comprising the lyoprotectant in a concentration of from about 0.5% to about 5% (w/v).

28. The composition of claim 27, wherein the aqueous composition comprises the lyoprotectant in a concentration of from about 1% to about 4%.

29. The composition of claim 28, wherein the aqueous composition comprises the lyoprotectant in a concentration of from about 1% to about 3%.

30. The composition of claim 3, wherein the freeze dried composition was prepared from an aqueous composition comprising a lyoprotectant in a concentration of from about 0.5% to 5% (w/v).

31. The composition of claim 30, wherein the freeze dried composition was prepared from an aqueous composition comprising a lyoprotectant in a concentration of from about 1% to 4%.

32. The composition of claim 31, wherein the freeze dried composition was prepared from an aqueous composition comprising a lyoprotectant in a concentration of from about 1% to 3%.

33. The composition of claim 24, further defined as comprising both a lyoprotectant and a cryoprotectant.

34. An aqueous pharmaceutical adenovirus composition comprising a polyol in an amount effective to promote the maintenance of adenoviral infectivity.

35. The composition of claim 34, further defined as maintaining an infectivity of about 70% PFU/mL to about 99.9% PFU/mL of the starting infectivity when stored for six months at 4° centigrade.

36. The composition of claim 34, further defined as maintaining an infectivity of about 80% to 95% PFU/mL of the starting infectivity when stored for six months at 4° centigrade.

37. The composition of claim 34, wherein said polyol is glycerol, propylene glycol, polyethylene glycol, sorbitol or mannitol.

38. The composition of claim 34, wherein said polyol concentration is from about 5% to about 30% (w/v).

39. The composition of claim 38, wherein said polyol concentration is from about 10% to about 30%.

40. The composition of claim 34, wherein said polyol is glycerol, included in a concentration of from about 10% to about 30% (w/v).

41. The composition of claim 34, wherein said composition further comprises an excipient in addition to said polyol, wherein said excipient is inositol, lactitol, xylitol, isomaltol, gelatin, agar, pectin, casein, dried skim milk, dried whole milk, silicate, carboxypolymethylene, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methhylcellulose, methylcellulose, sucrose, dextrose, lactose, trehalose, glucose, maltose, niacinamide, creatinine, monosodium glutamate dimethyl sulfoxide, sweet whey solids, human serum albumin, bovine serum albumin, PEG, glycine, arginine, proline, lysine, alanine, polyvinyl pyrrolidine, polyvinyl alcohol, polydextran, maltodextrins, hydroxypropyl-beta-cyclodextrin, partially hydrolysed starches, Tween-20 or Tween-80.

42. The composition of claim 41, wherein said composition further comprises at least a first and second of said excipients, said second excipient different from said first excipient.

43. A method for preparation of a long-term, storage stable adenovirus formulation, comprising the steps of:

5 (a) providing adenovirus and combining said adenovirus with a solution comprising a buffer, a bulking agent, a cryoprotectant and a lyoprotectant; and

(b) lyophilizing said solution,

10

whereby lyophilization of said solution produces a freeze-dried cake of said adenovirus formulation that retains high infectivity and low residual moisture.

44. The method of claim 43, wherein said bulking agent is mannitol, inositol, lactitol, xylitol, isomaltol, sorbitol, gelatin, agar, pectin, casein, dried skim milk, dried whole milk, silcate, carboxypolymethylene, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methhylcellulose or methylcellulose.

15

45. The method of claim 44, wherein said bulking agent is mannitol.

20

46. The method of claim 45, wherein mannitol comprises about 0.5% to about 8% (w/v) of said formulation.

47. The method of claim 43, wherein said cryoprotectant is sucrose, dextrose, lactose, trehalose, glucose, maltose, niacinamide, creatinine, monosodium glutamate dimethyl sulfoxide or sweet whey solids.

25

48. The method of claim 47, wherein said cryoprotectant is sucrose.

49. The method of claim 43, wherein said sucrose comprises about 2.5% to about 10% (w/v) of said formulation.

50. The method of claim 43, wherein said lyoprotectant is human serum albumin, bovine serum albumin, PEG, glycine, arginine, proline, lysine, alanine, polyvinyl pyrrolidine, polyvinyl alcohol, polydextran, maltodextrins, hydroxypropyl-beta-cyclodextrin, partially hydrolysed starches, Tween-20 or Tween-80.

51. The method of claim 50, wherein said lyoprotectant is human serum albumin.

52. The method of claim 43, wherein said buffer is Tris-HCl, TES, HEPES, mono-Tris, brucine tetrahydrate, EPPS, tricine, or histidine.

53. The method of claim 52, wherein said buffer is present in said formulation at a concentration at about 1 mM to 50 mM.

54. The method of claim 53, wherein said buffer is Tris-HCl.

55. The method of claim 54, wherein said Tris-HCl is included in a concentration of from about 1 mM to about 50 mM.

56. The method of claim 55, wherein said Tris-HCl is included in a concentration of from about 5 mM to about 20 mM.

57. The method of claim 43, further comprising a salt selected from the group consisting of $MgCl_2$, $MnCl_2$, $CaCl_2$, $ZnCl_2$, NaCl and KCl.

58. The method of claim 43, wherein said lyophilizing is carried out in the presence of an inert gas.

59. The method of claim 43, wherein lyophilizing said solution comprises the steps of:

- 5 (a) freezing said solution;
- (b) subjecting said solution to a vacuum; and
- (c) subjecting said solution to at least a first and a second drying cycle,

whereby said second drying cycle reduces the residual moisture content of said freeze-dried cake to less than about 2%.

10

60. A method for the preparation of a long-term storage, stable adenovirus liquid formulation, comprising the steps of providing adenovirus and combining said adenovirus with a solution comprising a buffer and a polyol, whereby said adenovirus liquid formulation retains high infectivity.

15